

I. AMENDMENTS

IA. AMENDMENTS TO THE SPECIFICATION

Please enter the following amendments to the specification.

1) Please amend paragraph 00233 on page 61, as follows:

Serine proteases can be categorized into the following ~~four~~ groups: trypsin-like serine proteases, which cleave at the carboxyl side of basic residues (i.e., Arg or Lys), chymotrypsin-like serine proteases, which cleave at the carboxyl side of aromatic side chains (i.e., Phe or Trp) and of hydrophobic residues with larger side chain (i.e., Met), and elastase-like serine proteases, which cleave at the carboxyl side of hydrophobic residues (i.e., Ala or Val). To test the specificity of the apoE cleavage enzyme, we incubated many tri- or tetra-peptides with Arg/Lys, Phe, or Val/Ala at the C-terminal end, which are potential substrates for trypsin-like, chymotrypsin-like, and elastase-like serine proteases, respectively, with roughly purified apoE cleavage enzyme.

2) Please amend paragraph 00140, beginning on page 33, as follows:

In some embodiments, the invention provides compositions comprising an inhibitor of an enzyme that catalyzes the formation of carboxyl-terminal truncated apoE and at least one other therapeutic agent. Agents that inhibit an apoE cleavage enzyme are described above. Other therapeutic agents that can be formulated together with an inhibitor of an enzyme that catalyzes the formation of carboxyl-terminal truncated apoE include, but are not limited to, agents that are used to treat individuals with AD, including, but not limited to, acetylcholinesterase inhibitors, including, but not limited to, ~~Aricept~~ Aricept® (donepezil), ~~Exelon~~ Exelon® (rivastigmine), metrifonate, and tacrine (~~Cognex~~) (Cognex™); non-steroidal anti-inflammatory agents, including, but not limited to, ibuprofen and indomethacin; cyclooxygenase-2 (Cox2) inhibitors such as Celebrex; and monoamine oxidase inhibitors, such as Selegilene (Eldepryl or Deprenyl). Any known inhibitor of chymotrypsin-like serine proteases can be formulated together with another therapeutic agent used to treat AD. Dosages for each of the above agents are known in the art, and can be used in a pharmaceutical preparation with an apoE

cleavage enzyme inhibitor. For example, ~~Aricept~~ Aricept® is generally administered at 50 mg orally per day for 6 weeks, and, if well tolerated by the individual, at 10 mg per day thereafter.